Meniscal fibrocartilaginous structures are subject to numerous stresses when performing its necessary functions to maintain intra-articular homeostasis. Pathological events causing a loss of tissue integrity will result in meniscal dysfunction, which will inevitably lead to the debilitating disease of osteoarthritis. When working to characterize osteoarthritic meniscal pathology, it was evident that the clinical assessment of radiography will correlate with gross and histologic measures of disease. These three scoring methods correlated well with the biochemical and molecular changes that occur when comparing normal to osteoarthritic menisci and medial to lateral osteoarthritic menisci. In order to more fully differentiate the abundant transformations that occur between aged-normal, meniscectomy, and osteoarthritic menisci, microarray and mass spectrometry analyses were utilized. Pathologic menisci appeared to haphazardly attempt an increase of its extracellular matrix components, some captivating markers of vascularity were increased, and a protein of potential therapeutic value was identified. Proteomic analysis was further utilized to study synovial fluid markers associated with meniscal disease and was able to identify a number of proteins with biomarker potential and a few additional proteins of therapeutic significance. These studies identified novel data that help to define the pathological changes a meniscus undergoes upon degradation.